



2012 IAPAC ADHERENCE GUIDELINES: ADDRESSING THE ACHILLES'S HEEL OF TasP and PreP

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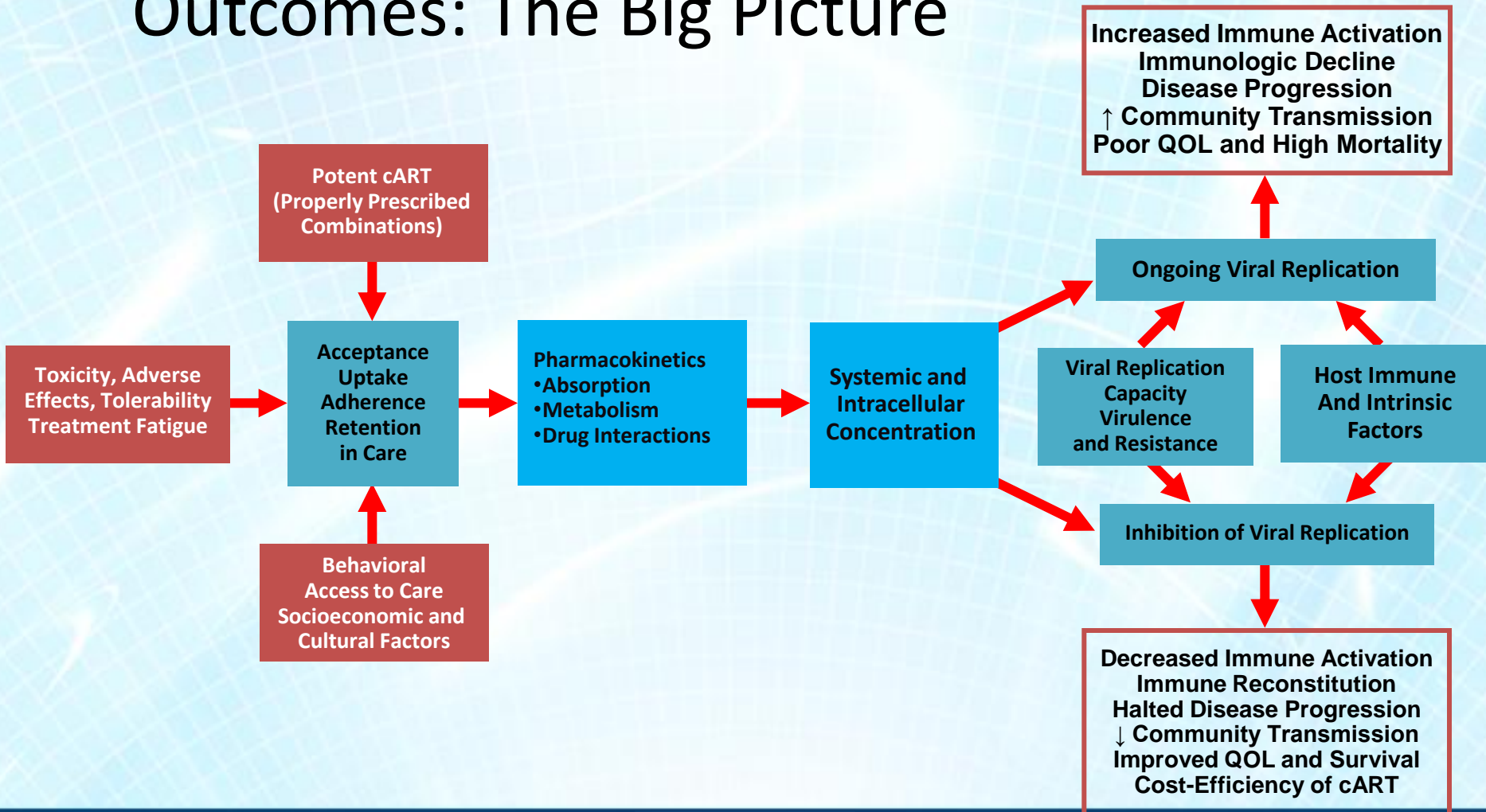
Stellenbosch University, Dept of Medicine and Center for Infectious Diseases,

Cape Town, South Africa

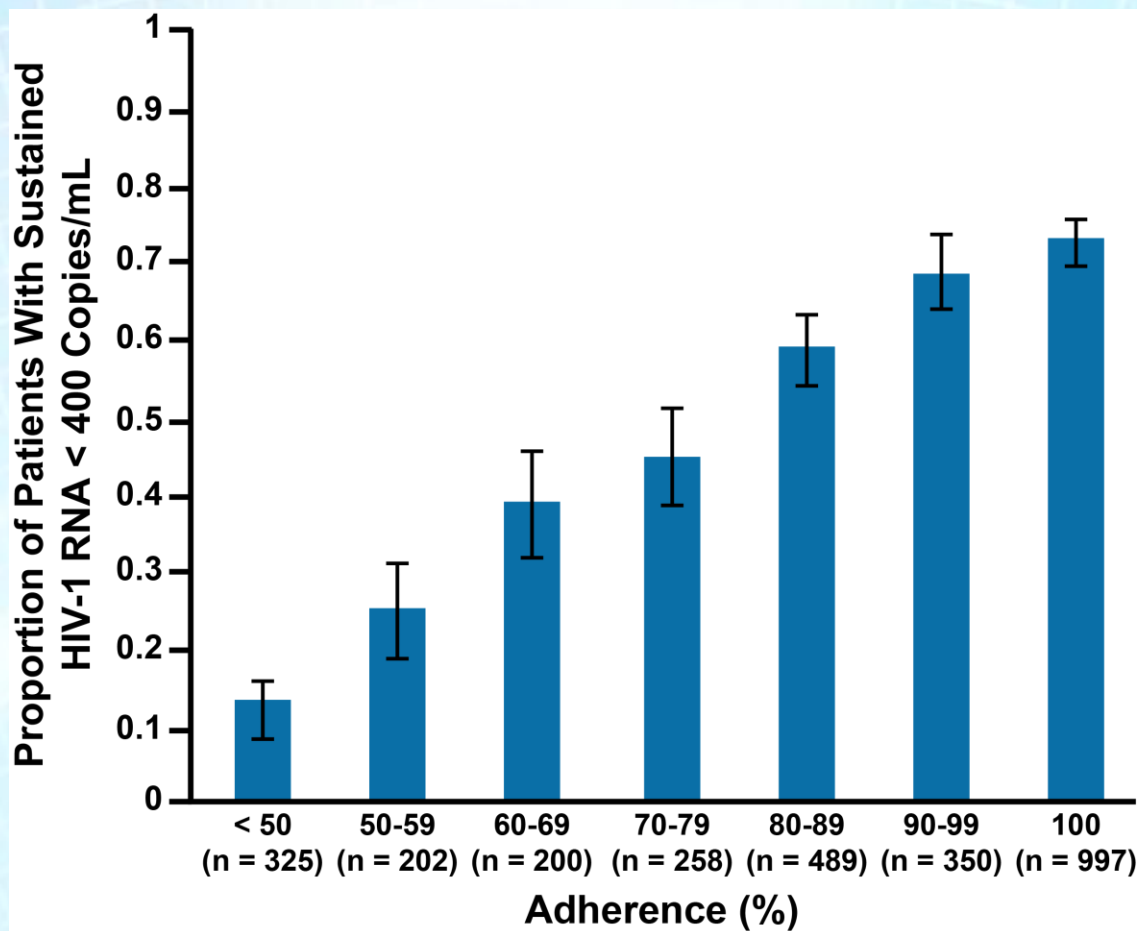
ROAD MAP

- Background
- Methodology
- Grading scales for the quality of evidence and strength of recommendations
- Recommendations
- Acknowledgments

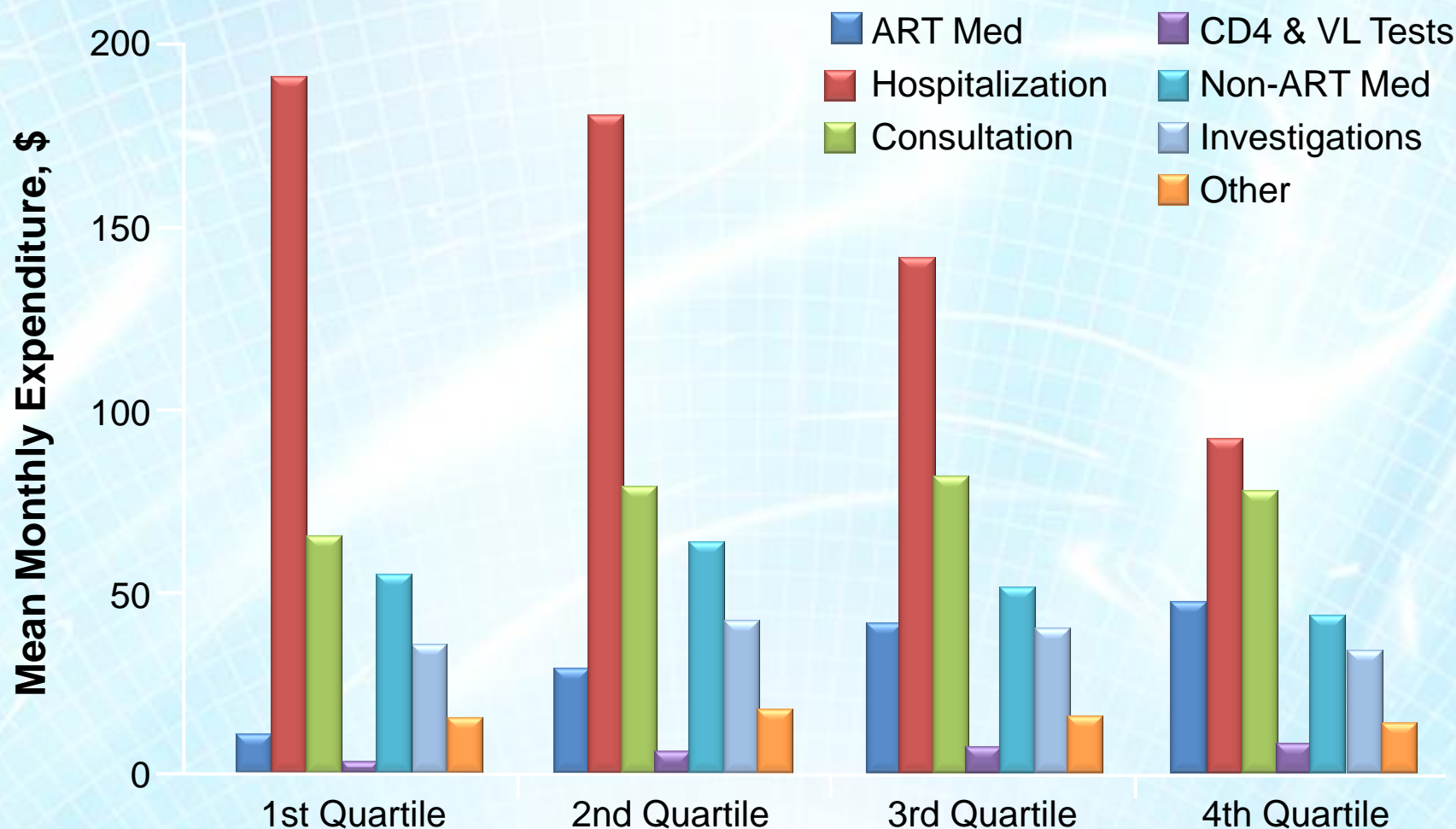
Key Determinants of HIV Treatment Success and Outcomes: The Big Picture



ART Adherence Predicts Virologic Response in Dose-Response Fashion

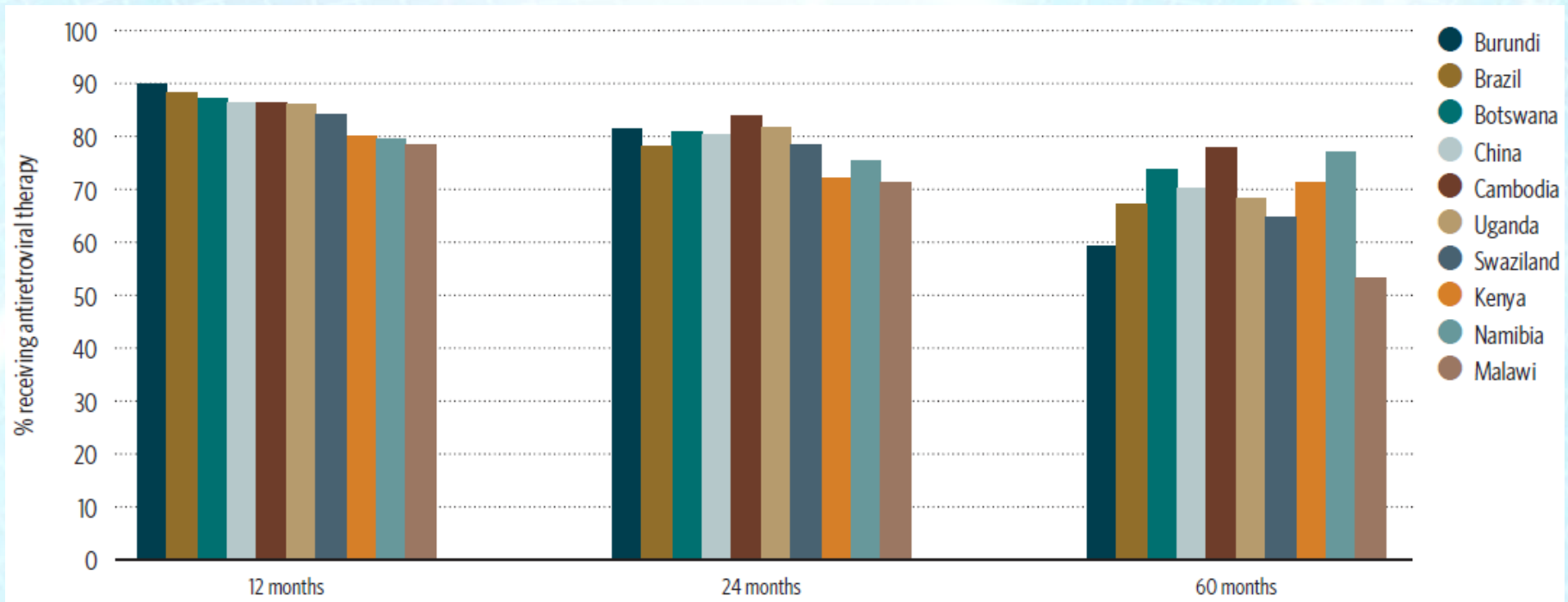


Adherence to ART Reduces Overall Health Care Costs



Pharmacy Claim Adherence

RETENTION RATES AFTER STARTING ANTIRETROVIRAL THERAPY IN THE SOUTH



WHO, Global HIV/AIDS Response, 2011



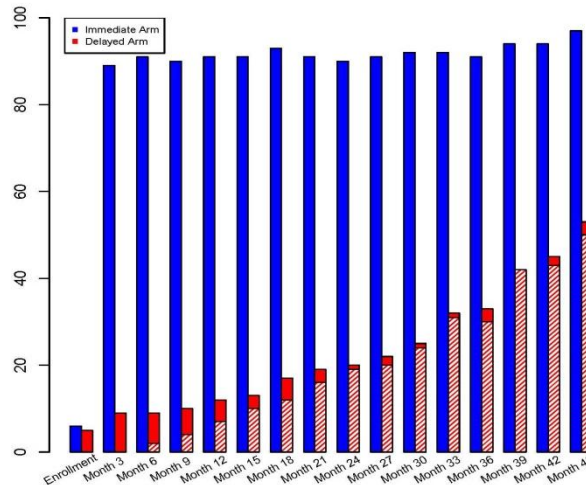
REAL-WORLD VS. TRIAL SETTING ART ADHERENCE LEVELS

- Systematic review of adherence (Mills, Nachega et al JAMA 2006)
 - 28,689 patients in 228 studies

Resource-Rich Country
54.7% (95 CI: 48.0-61.3%)

Resource-Poor Country
77.1% (95 CI: 67.3-85.6%)

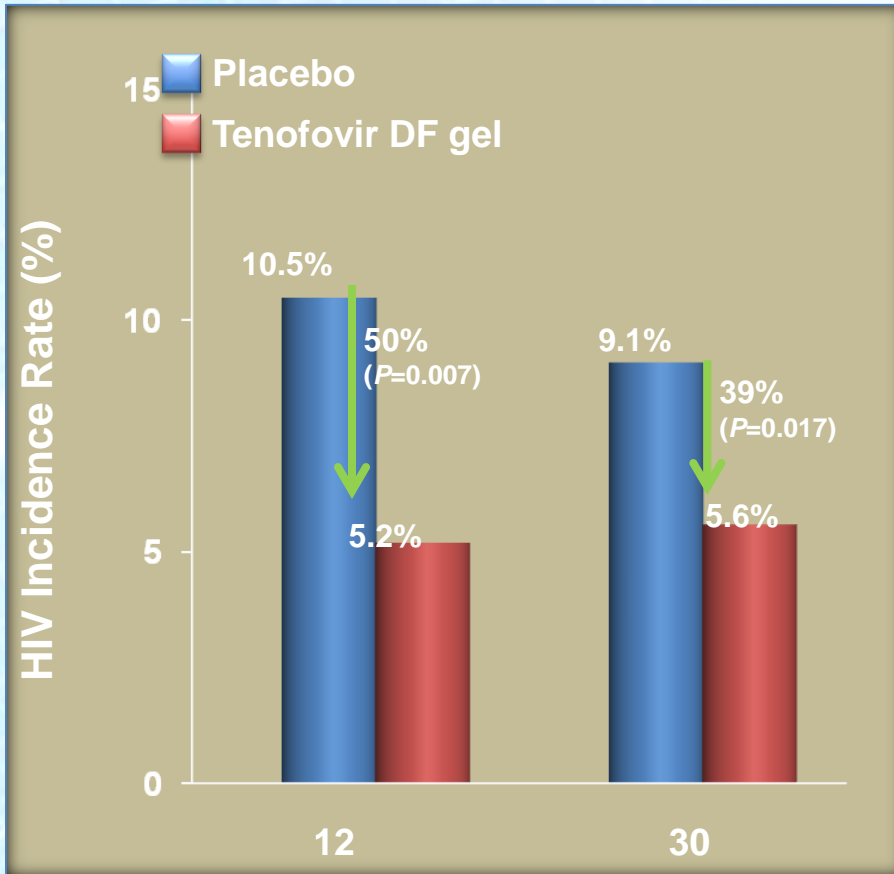
Contrast to HPTN 052



Cohen M. et al. NEJM 2011

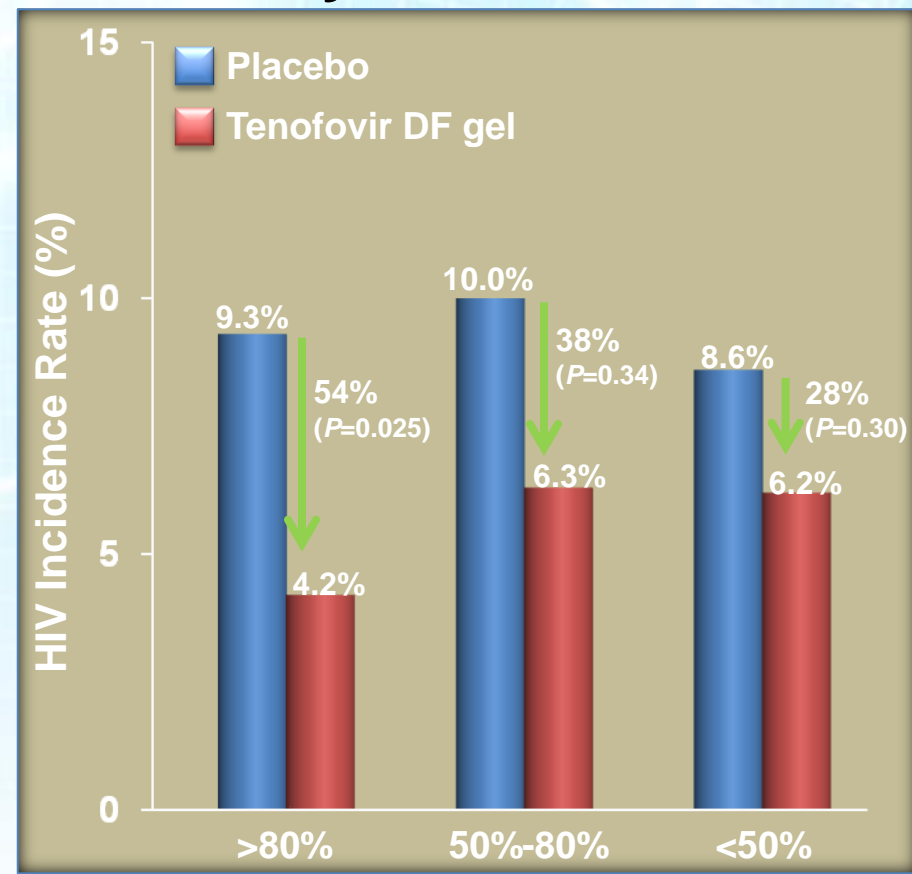
CAPRISA 004 Results: HIV Incidence

Overall



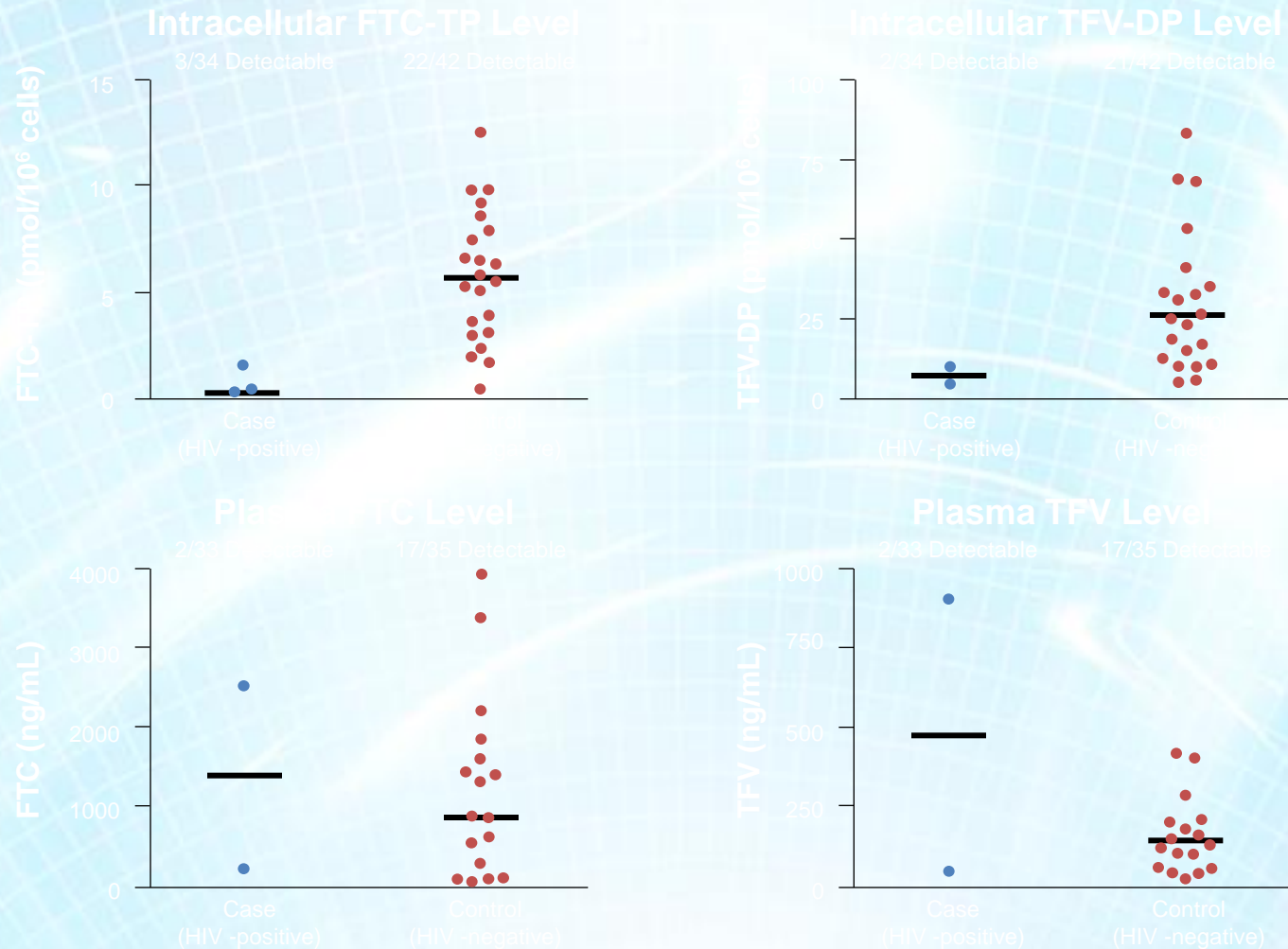
Follow-Up (months)

By Adherence



Adherence Level (months)

iPrEX: Drug Levels Are a Strong Correlate of Protection



- 92% reduction in risk *with* adequate drug levels (OR 12.9, P <.001)

BACKGROUND (continued)

- To date, there has not been a full evaluation of the evidence base for how to best monitor or support engagement in HIV care and ART adherence.
- These guidelines are evidence-based recommendations to help providers optimize entry into and retention in care and support ART adherence for people living with HIV.

2012 Guidelines for Improving Entry and Retention in Care & ART Adherence for Persons



**With HIV: Evidence-Based
Recommendations From an International Association of
Physicians in
AIDS Care Panel—Funding from NIH/OAR**

**Melanie A. Thompson, MD; Michael J. Mugavero, MD, MHSc;
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METHODS

- A systematic literature search was conducted to produce an evidence base restricted to randomized controlled trials (RCTs) and observational studies **with comparators** that had at least 1 measured biological or behavioral endpoint.
- A total of **325 studies** met the criteria.
- Panel members drafted recommendations based on the **body of evidence** for each method or intervention and then **graded the overall quality of the body of evidence** and strength for each recommendation.

GRADING SCALE: QUALITY OF EVIDENCE

Quality or Strength	Interpretation
Excellent (I)	RCT evidence without important limitations Overwhelming evidence from observational studies
High (II)	Strong evidence from RCT with important limitations Strong evidence from observational studies
Medium (III)	RCT evidence with critical limitations Observational study evidence without important limitations
Low (IV)	Observational study evidence with important or critical limitations

GRADING SCALE: STRENGTH OF RECOMMENDATION

Strength	Interpretation
Strong (A)	Almost all patients should receive the recommended course of action
Moderate (B)	Most patients should receive the recommended course of action. However, other choices may be appropriate for some patients
Optional (C)	There may be consideration for this recommendation on the basis of individual circumstances. Not recommended routinely

WHAT TOPICS THESE GUIDELINES ADDRESS

- Entry and retention in HIV care
- Monitoring ART adherence
- Interventions to improve ART Adherence
- Adherence tools for patients
- Education and counseling interventions
- Health system and service delivery interventions
- Special populations (Pregnancy, Substance Abuse, Mental Health, Incarceration, Homeless, Children/Adolescents)

RECOMMENDATIONS: ENTRY INTO/RETENTION IN CARE

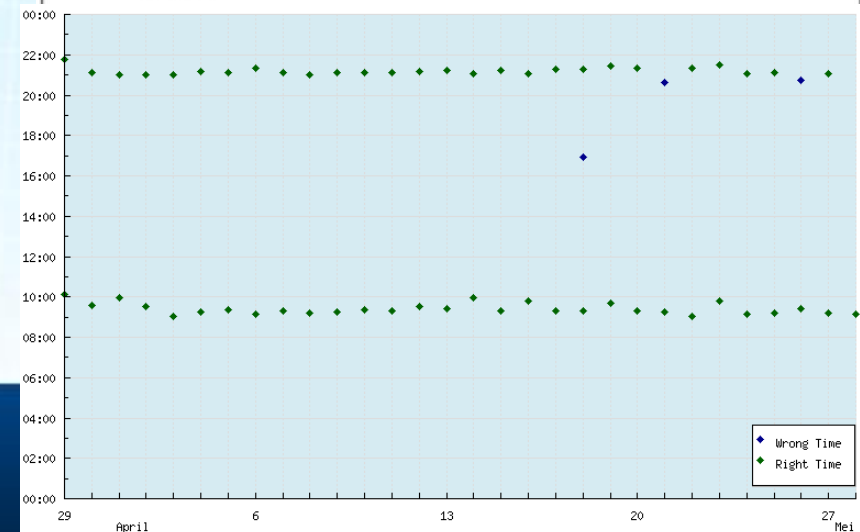
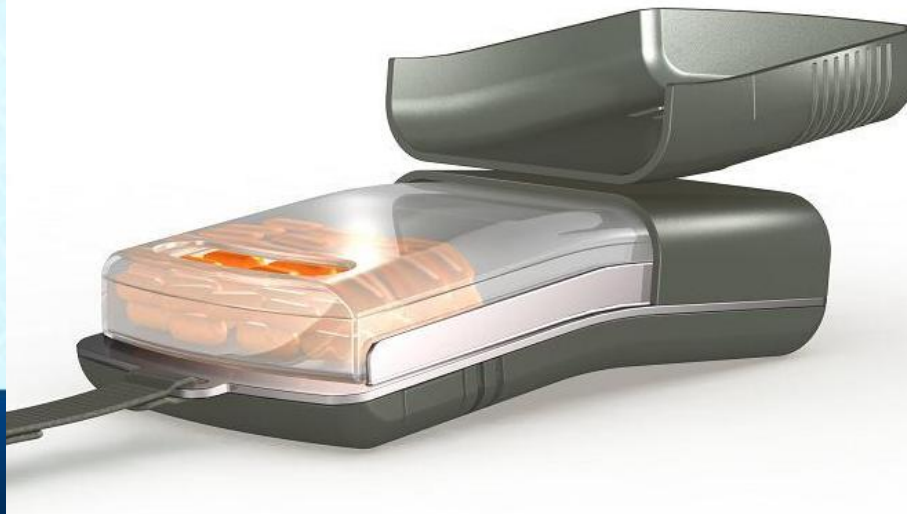
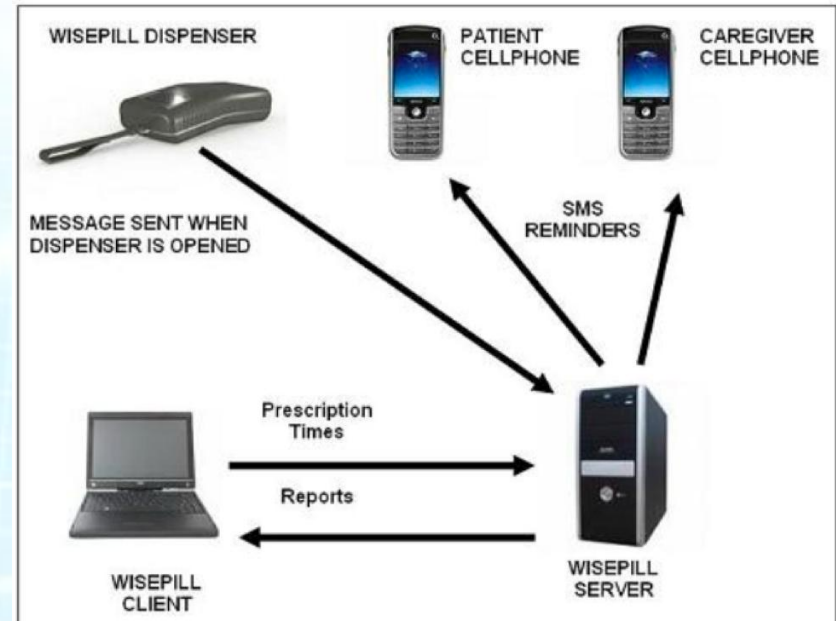
- Systematic **monitoring** of successful **entry into HIV care** is recommended for all individuals diagnosed with HIV (II A).
- Systematic **monitoring of retention** in HIV care is recommended for all patients (II A).
- **Brief, strengths-based case management** for individuals with a new HIV diagnosis is recommended (II B).
- **Intensive outreach** for individuals not engaged in medical care within 6 months of a new HIV diagnosis may be considered (III C).
- **Use of peer or paraprofessional** patient navigators may be considered (III C).

RECOMMENDATIONS: MONITORING ART ADHERENCE

- **Self-reported** adherence should be obtained routinely in all patients (**II A**).
- **Pharmacy refill data** are recommended for adherence monitoring when medication refills are not automatically sent to patients (**II B**).
- **Drug concentrations** in biological samples **are not** routinely recommended (**III C**).
- **Pill counts** performed by staff or patients are not routinely recommended (**III C**).
- **Electronic drug monitors (EDMs)** **are not** routinely recommended for clinical use (**I C**).

Real-time Adherence Monitoring

Bangsberg & Deeks Annal Int Med 2010



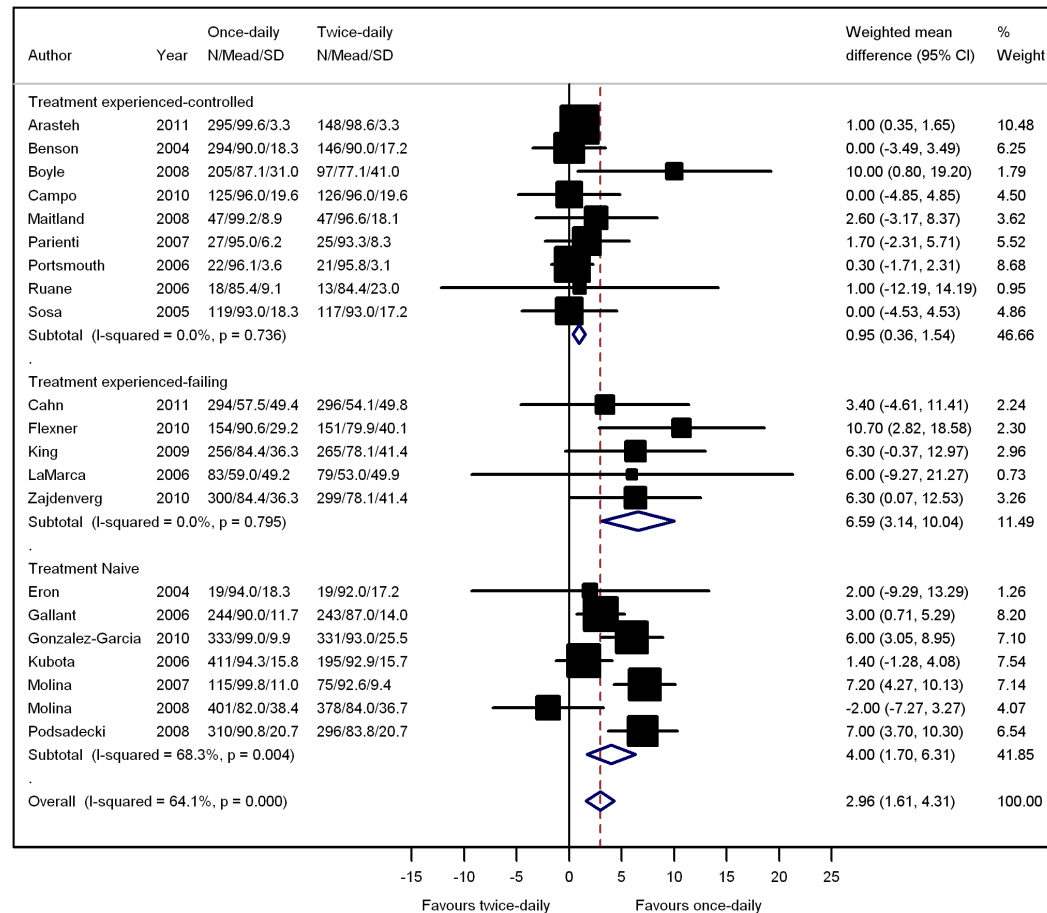
RECOMMENDATIONS: ART STRATEGIES

- Among regimens of similar efficacy and tolerability, **once-daily (QD) regimens** are recommended for **treatment-naïve** patients beginning ART (**II B**).
- **Switching treatment-experienced** patients receiving complex or poorly tolerated regimens to **once-daily (QD) regimens** is recommended, given regimens with equivalent efficacy (**III B**).
- Among regimens of **equal efficacy and safety**, **fixed-dose combinations** are recommended to decrease pill burden (**III B**).

1997-2011: The long Road to QD ART Regimen, Patient Satisfaction and Adherence



Effect of QD vs BID ARV regimens on the rate of adherence



RECOMMENDATIONS: ADHERENCE TOOLS FOR PATIENTS

- Reminder devices and use of communication technologies with an interactive component are recommended (**I B**).
- Education and counselling using specific adherence-related tools is recommended (**I A**).

**Mobile phone technologies improve adherence to
antiretroviral treatment in a resource-limited setting:
a randomized controlled trial of text
message reminders**

Cristian Pop-Eleches^{a,b,*}, Harsha Thirumurthy^{c,d,*},
James P. Habyarimana^{e,*}, Joshua G. Zivin^f, Markus P. Goldstein^g,
Damien de Walque^g, Leslie MacKeen^h, Jessica Haberer^{i,o},
Sylvester Kimaiyo^j, John Sidle^{k,l}, Duncan Ngare^m and
David R. Bangsberg^{n,p}

**Effects of a mobile phone short message service on
antiretroviral treatment adherence in Kenya
(WelTel Kenya1): a randomised trial**

*Richard T Lester, Paul Ritvo, Edward J Mills, Antony Kariri, Sarah Karanja, Michael H Chung, William Jack, James Habyarimana,
Mohsen Sadatsafavi, Mehdi Najafzadeh, Carlo A Marra, Benson Estambale, Elizabeth Ngugi, T Blake Ball, Lehana Thabane, Lawrence J Gelmon,
Joshua Kimani, Marta Ackers, Francis A Plummer*



*WELTEL PROTOCOL: SMS TEXT MESSAGING



**SMS: "Mambo?"
= How RU?"**

SMS 'check-in'

Monday

**"Sawa" = Fine
"Shida" = Problem**



If necessary



**Health
Advice**



<48h

SMS response

*Derived from **focused group discussions** with HCW and patients

PRACTICAL APPLICATIONS*: ADHERENCE TOOLS FOR PATIENTS

- Adherence **tools** may be more beneficial when combined with education or counseling.
- Studies have evaluated **pillboxes, dose planners, reminder alarm device, and EDMs** and most found positive effects on adherence.

*Practical applications of A-level recommendations

Results: Pill box organizers improve adherence and reduce viral load

<u>MSM Estimator</u>	<u>Difference in % Adherence</u>	<u>95% CI</u>	<u>Difference in Log VL</u>	<u>95% CI</u>	<u>OR VL<400</u>	<u>95% CI</u>
G-Comp	4.5%	(2.0, 7.0)	-0.34	(0.08, 0.60)	1.81	(1.25, 2.62)
IPTW	4.1%	(0.0, 8.3)	-0.37	(0.05, 0.69)	1.91	(1.27, 2.90)
Double Robust	4.1%	(1.1, 7.1)	-0.36	(0.09, 0.63)	1.91	(1.27, 2.90)

- 4% better adherence
- 1.9 odds better viral suppression
- \$5.00/pill box: extremely cost-effective intervention
- Should be standard-of-care

RECOMMENDATIONS: EDUCATION/COUNSELING

- Individual one-on-one ART education is recommended (II A).
- Providing one-on-one adherence support to patients through 1 or more adherence counselling approaches is recommended (II A).
- Group education and group counselling are recommended; however, the type of group format, content, and implementation cannot be specified on the basis of the currently available evidence (II C).
- Multidisciplinary education and counselling intervention approaches are recommended (III B).
- Offering peer support may be considered (III C).

RECOMMENDATIONS: HEALTH SYSTEM/SERVICE DELIVERY

- Using **nurse- or community counsellor-based care** has adherence and biological outcomes similar to those of doctor- or clinic counsellor-based care and is recommended in under-resourced settings (**II B**).
- Interventions providing **case management services** and resources to address food insecurity, housing, and transportation needs are recommended (**III B**).
- Integration of **medication management services into pharmacy systems** may be considered (**III C**).
- Directly administered ART **is not** recommended for routine clinical care settings (**I A**).

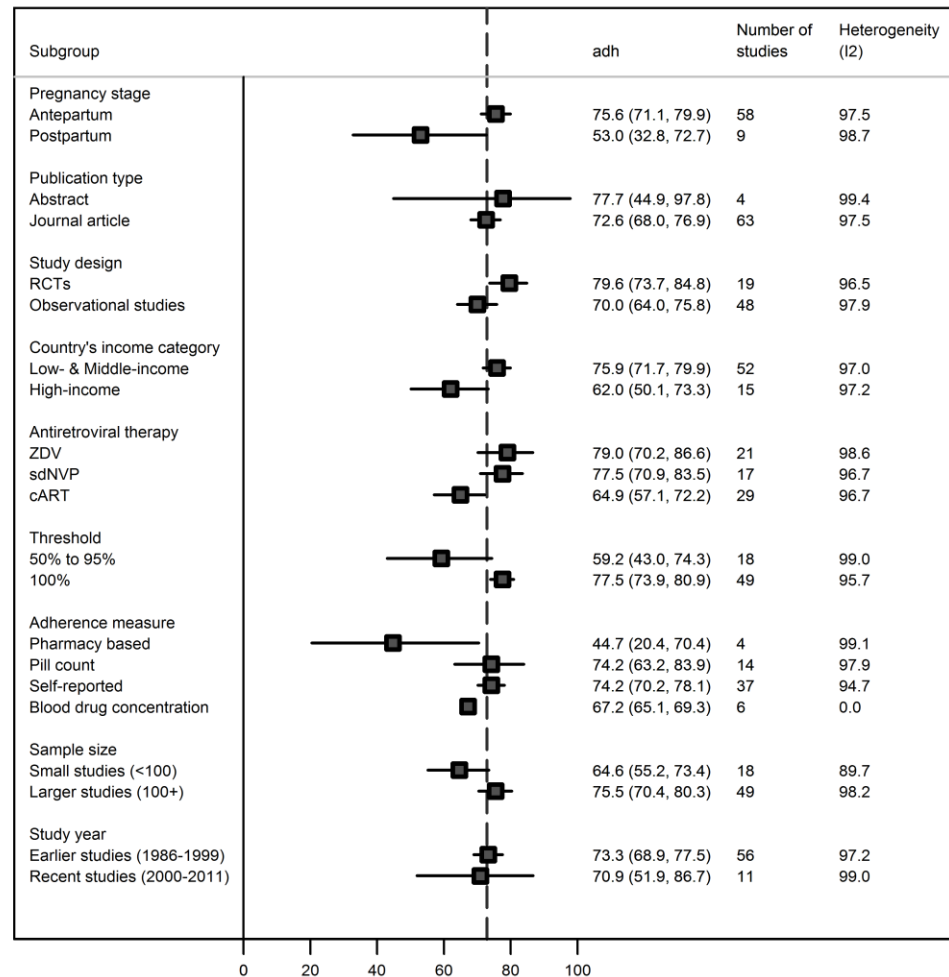
A RANDOMIZED CONTROLLED TRIAL COMPARING THE EFFECTS OF COUNSELING AND/OR REMINDER DEVICE ON ART ADHERENCE & VL



➤ ART adherence counseling decreases virological failure by over 50%

- 2 standardized counseling sessions prior to ART and 1 educational adherence session after 1 month of ART vs. SOC (1 baseline session)/FUP 18 mos
- Topics covered:
 - HIV + CD4 counts
 - Side effects of drugs
 - Importance of adherence
- Approach:
 - Trained counselors
 - Discussed approaches to overcoming barriers
 - Developed trusting relationship between patient and clinic

ART ADHERENCE IN PREGNANCY & POST-PARTUM: A META-ANALYSIS



RECOMMENDATIONS: PREGNANT WOMEN

- Targeted PMTCT treatment (including HIV testing and serostatus awareness) improves adherence to ART for PMTCT and is recommended compared with an untargeted approach (**treatment without HIV testing**) in high HIV prevalence settings (**III B**)
- **Labor ward-based PMTCT adherence services** are recommended for women who are not receiving ART before labor (**II B**)

RECOMMENDATIONS: SUBSTANCE USE DISORDERS

- Offering **buprenorphine** or **methadone** to opioid-dependent patients is recommended (**II A**).
- **Directly administered ART (DAART)** is recommended for individuals with substance use disorders (**I B**).
- Integration of **DAART into methadone maintenance treatment** for opioid-dependent patients is recommended (**II B**).

RECOMMENDATION: MENTAL HEALTH

- Screening, management, and treatment for depression and other mental illnesses in combination with adherence counselling are recommended (**II A**).

RECOMMENDATION: INCARCERATION

- **DAART** is recommended during incarceration (**III B**) and may be considered upon release to the community (**II C**).

RECOMMENDATIONS: HOMELESS/MARGINALLY HOUSED INDIVIDUALS

- **Case management** is recommended to mitigate multiple adherence barriers in the homeless (**III B**).
- **Pillbox organizers** are recommended for persons who are homeless (**II A**).

RECOMMENDATIONS: CHILDREN/ADOLESCENTS

- **Intensive youth-focused case management** is recommended for adolescents and young adults living with HIV to improve entry into and retention in care (**IV B**).
- Pediatric- and adolescent-focused therapeutic support interventions using **problem-solving approaches** and addressing psychosocial context are recommended (**III B**).
- **Pill-swallowing training** is recommended and may be particularly helpful for younger patients (**IV B**).
- **DAART** improves short-term treatment outcomes and may be considered in pediatric and adolescent patients (**IV C**).

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THANK YOU

